REMARKS

Claims 51-68 were pending in the present application. Claims 51-68 have been canceled herein and replaced with new claims 69-100. Upon entry of the present amendment, claims 69-100 will remain pending.

Applicants' representatives Jason Ferrone and Mark Roach thank Examiners Moran and Miller for granting an interview ("Interview") on May 19, 2005 upon short notice. Applicants' representatives communicated that an RCE would be filed with new claims, which were discussed. The Examiners suggested that the method claims may be looked upon more favorably than the "service" claims. Applicants further communicated that a supplemental IDS would be filed after the filing of the RCE.

The title of the application has been amended herein to more accurately describe the invention presently claimed.

I. Support for the New Claims

Measuring the molecular mass of a 46-mer amplification product is indicated in Figure 6 and described at, for example, page 26, line 15 of the specification. Calculating molecular masses of amplification products is indicated in, for example, Table 2, page 26 of the specification.

The claims now recite that the amplification products are 46 to 166 nucleobases in length in order to further define the product compositions of the database as suggested by the Examiners in the Interview. As stated in Brief Description of the Figures, with reference to Figures 1A-1I, (depicting 16S rRNA and 23S rRNA consensus sequences and priming regions) on page 9, lines 22-23 of the specification: "lines with arrows are examples of regions to which the primer pairs for PCR are designed."

Support for an amplification product 46 nucleobases in length exists in, for example, Figure 1A-2 wherein the combination of a first arrow drawn from nucleobase positions 1337-1352 and a second arrow drawn from nucleobase positions 1369-1382 indicate that the amplification product corresponds to positions 1337 to 1382 – an amplification product length of 46 nucleobases.

Support for an amplification product 166 nucleobases in length exists in, for example,

Figure 1B-2 wherein the combination of a first arrow drawn from nucleobase positions 109-120 and a second arrow drawn from nucleobase positions 252-274 indicate that the amplification product corresponds to positions 109-274 – an amplification product length of 166 nucleobases.

Furthermore, as shown in the table below, several other priming regions of 16S ribosomal RNA are indicated in Figure 1A. Thus, there are 12 priming regions shown which produce amplification products ranging in length from 46 to 166 nucleobases for 16S rRNA alone.

Start Position	End Position	Amplicon Length
51	120	70
109	274	166
252	332	81
557	704	148
714	805	92
787	894	108
971	1062	92
1100	1188	89
1228	1310	83
1294	1353	60
1337	1382	46
1391	1541	151

Additional priming regions producing amplification products within this range are also indicated for the 23S rRNA structures shown in Figures 1C-1, 1C-2, 1D, 1E, 1F, 1G, and 1H.

The claims now recite a method that includes the step of measuring or calculating a plurality of molecular masses (claim 69) or base compositions (claim 85) of amplification products obtained with a primer pair that hybridizes to nucleic acid of about one hundred or more bacterial bioagents, support for which can be found at, for example, page 15, line 3 of the specification.

Support for providing a database comprising at least some members of measured or calculated molecular masses with indexing to bacterial bioagent characterizing information (species name, for example) is indicated in, for example, Table 2, page 26 of the specification.

Support for interrogating the database with an identification query and delivering a response is indicated in, for example, original claim 17.

Support for new claims 70 and 86 wherein nucleic acid encodes ribosomal RNA or a protein involved in translation, replication, recombination, repair, transcription, nucleotide metabolism, amino acid metabolism, lipid metabolism, energy generation, uptake, or secretion is indicated at, for example, page 12, lines 1-4 (proteins) and page 13, lines 10-14 (ribosomal RNA) of the specification.

Support for new claims 71-73 and 87-89 wherein the bioagent characterizing information is a genus name or a species name is indicated in, for example, Table 2.

Support for new claims 74 and 90 wherein the bioagent characterizing information is a strain name is found at, for example, page 29, lines 9-12 of the specification where it is indicated that species repeated in Table 5 are different strains which have different base compositions.

Support for new claims 75-76 and 91-92 wherein the response is delivered via a network is found in, for example, Examples 12-14 and in original claims 23-25 of the specification.

Support for new claims 77-78 and 93-94 wherein the molecular mass is determined by mass spectrometry is found at, for example, page 18, lines 20-27 of the specification.

Support for new claims 79 and 95 wherein the variable region has no greater than 5% sequence identity is found at, for example, page 15, lines 6-7 of the specification.

Support for new claims 80-81 and 96-97 wherein the primer pair comprises at least one chemical modification, is found at, for example, page 15, lines 28-30 and page, lines 1-5 of the specification.

Support for new claims 82-83 and 98-99 wherein the bacterial bioagent is a biological warfare agent is found at, for example, page 16, lines 6-14 of the specification.

Support for new claims 84 and 100 wherein the conserved regions have between 80-100% sequence identity is found at, for example, page 15, lines 3-4 of the specification.

II. The Claimed Invention Is Not Obvious

Claims 51, 65, and 67 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over the combination of Muddiman et al., Anal. Chem., 1997, 69, 1543-1549 (hereinafter, the "Muddimann I reference") or Muddiman et al., Anal. Chem., 1996, 68, 3705-3712 (hereinafter, the "Muddiman II reference") in view of Widjojoamodjo et al., J. Clin. Micro.,

1994, 32, 3002-3007 (hereinafter, the "Widjojoamodjo reference"). Additional claims are rejected over the previous combination in further view of several additional references that report cloning of particular housekeeping genes (e.g., Liu, Hermann, Love, Tong, Seshadri, Leif, Martemyanov, Takahashi, and Morse references). The Final Rejection states that it would have been obvious to modify the method of Muddiman to interrogate a database with information obtained by amplifying a variable region of a gene by using primers directed to conserved regions of a gene such as taught by Widjojoatmodjo, where the motivation would have been to determine the identity of bacteria without the need of a large panel of probes as taught by Widjojoatmodjo. To the extent that the rejection of the canceled claims may be applied to the new claims, Applicants traverse the rejection and respectfully request reconsideration because the combination of the cited references does not result in Applicants' claimed invention.

As a preliminary matter, Applicants note that the Final Rejection mischaracterizes the Widjojoatmodjo reference with respect to the alleged existence of a large panel of probes. The SSCP method employed in the Widjojoatmodjo reference does not employ a large panel of probes. Rather, silver staining is used to visualize SSCP bands on a gel (see "Detection of SSCP Patterns" col. 2 page 3003).

Applicants interpret the obviousness argument as meaning that the primers of the Widjojoatmodjo reference could be used to obtain amplification products of nucleic acid of bacterial bioagents which could be then analyzed by the mass spectrometry method of either the Muddiman I or II reference. Any method arrived at by combining the primers of the Widjojoatmodjo reference with the mass spectrometry method of either Muddiman reference is, however, not within the scope of the newly presented claims because the primers of the Widjojoatmodjo reference give rise to amplification products 216 bp and 255 bp in length (see page 3003, col. 1, lines 1-6).

Applicants note that the Final Rejection states that the Muddiman II reference employs primers that produce amplification products 89 bp in length. The primers of this Muddiman reference, however, do not hybridize to nucleic acid of about one hundred or more bacterial bioagents at conserved regions that flank an intervening variable region. Thus, the primers employed by the Muddiman II reference are also outside of the scope of the newly presented

claims.

The Final Rejection asserts that, with respect to Table 1 of the Widjojoatmodjo reference, "...all *Clostridium* species gave species-specific patterns when variable regions were amplified by using conserved primers, *i.e.* identity for any particular variable region among species was less than 5%." Applicants agree that all *Clostridium* species gave species specific PCR-SSCP patterns (patterns 4-14) but also wish to point out that it is evident that the Final Rejection equates a unique PCR-SSCP pattern with "identity" *i.e:* the PCR-SSCP pattern represents an identifier. In contrast, in the original claim 66, the original intent of Applicants was to convey that the variable region exhibits **no greater than 5% sequence identity** and have amended the claims in clarification of this original intent. The term "sequence identity" is well known in the arts of molecular biology and refers to the percentage of a nucleic acid sequence that is conserved.

The Widjojoatmodjo reference itself indicates that "PCR-SSCP is reported to be capable of detecting single-base mutations in a fragment of a few hundred base pairs..." (p. 3004, col 2, 1st paragraph). Thus, it is indicated that two distinct pattern identifiers may arise when two fragments differ by only a single base. These two distinct pattern identifiers will have greater than 5% sequence identity. For example, when two fragments, each of a length of 200 bases have a single base difference but are otherwise identical, the sequence identity between the first fragment and the second fragment will be 199/200 = 99.5% sequence identity. Clearly, the PCR-SSCP patterns are not indicative of **sequence identity of no greater than 5%**. Furthermore, there is no indication that sequence identity was examined in the Widjojoatmodjo reference for any part of any of the amplification products analyzed therein.

Thus, the claimed invention is not obvious in view of the combination of cited references. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. §103(a) be withdrawn.

III. The Claims Are Clear And Definite

Claims 51-68 are rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which

Applicants regard as their invention. Applicants respectfully request reconsideration in view of the new claims.

Claim 51 is allegedly unclear as to what limitation of a database (a product) is intended by the process. New independent claims have been drawn to more clearly define the contents of the database. The claims now recite a method that includes the step of measuring or calculating a plurality of molecular masses (claim 69) or base compositions (claim 85) of amplification products 46 to 166 nucleobases in length obtained with a primer pair that hybridizes to nucleic acid of about one hundred or more bacterial bioagents. Support for this claim element is found at, for example, page 15, line 3 of the specification.

Claim 51 is also allegedly unclear as to what limitation of the identification query is intended. New claims 69 and 85 now recite that the identification query comprises a molecular mass measurement (claim 69) or a base composition measurement (claim 85) of an amplification product 46 to 166 nucleobases in length of a bacterial bioagent obtained upon amplification with a primer pair. Applicants submit that the identification query of new claims 69 and 85 is clear and definite.

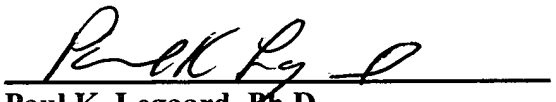
Claim 51 is also allegedly unclear as to whether Applicants intend the gene to *encode* a DNA polymerase III, etc. or to be a DNA polymerase III, etc. New claims 70 and 86 now indicate that the nucleic acid "encodes" ribosomal RNA or a protein involved in translation, replication, recombination, repair, transcription, nucleotide metabolism, amino acid metabolism, lipid metabolism, energy generation, uptake, or secretion.

In view of the foregoing, Applicants respectfully request that the rejection under 35 U.S.C. §112, second paragraph be withdrawn.

IV. Conclusion

Applicants submit that the pending claims are in condition for allowance. Applicants respectfully request that the Examiner contact Applicants' undersigned representative if such allowance is not forthcoming.

Respectfully submitted,



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